Electronic Supplementary Material (ESI) for RSC Advances.

Supplementary Information

Discovery of new BTK inhibitors with B cells suppression activity bearing a 4, 6-substituted thieno[3,2-*d*]pyrimidine scaffold

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Contents

HPLC methods for determine the purity of 4-20.

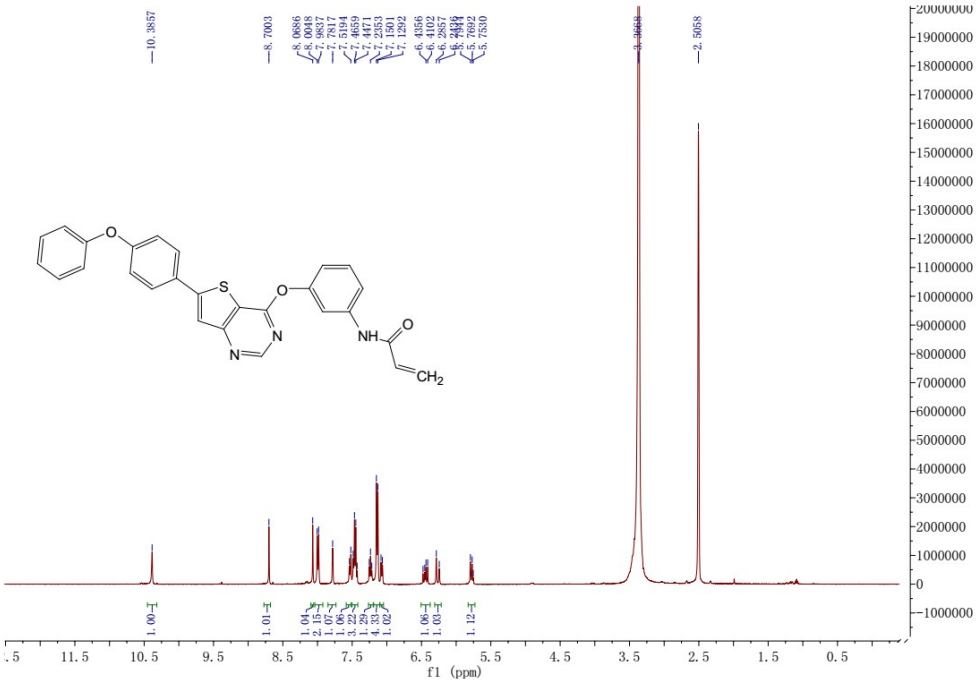
The purity of all tested compounds was established by HPLC to be > 95%. HPLC analysis was performed at room temperature using a Diamonsil C_{18} (250 mm × 4.6 mm).

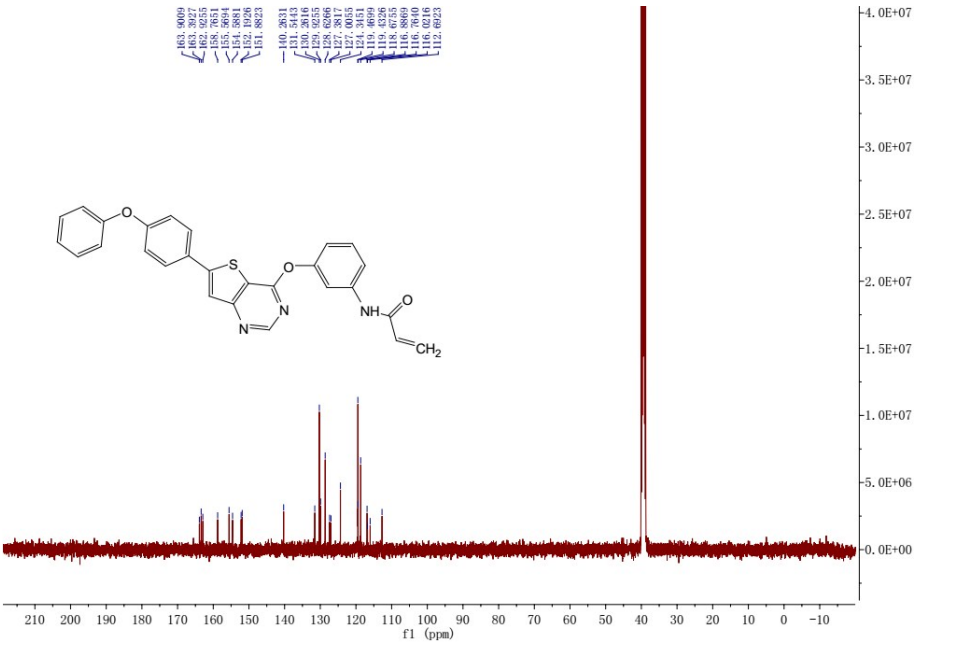
Method 1: A mobile phase gradient from 5% MeCN/water (10% MeOH /H_2O) to 95% MeCN/water (10% MeOH /H_2O) for 20 min, a flow rate of 1.0 mL/min. This method was used to determine the purity for compound **4**.

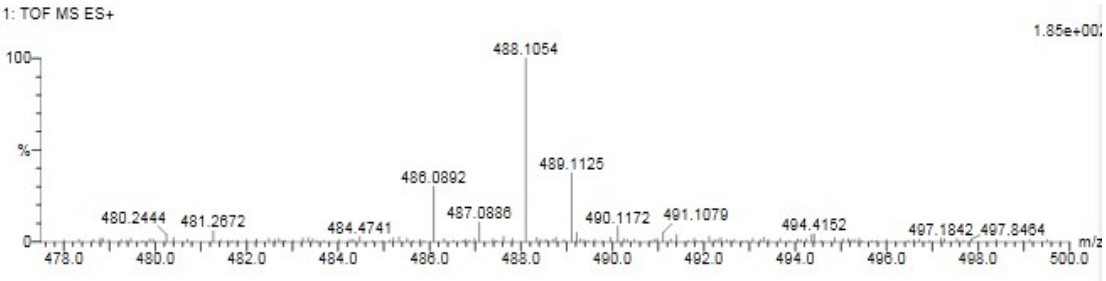
Method 2: A mobile phase gradient from 5% CH_3CN/ buffer (0.1% TFA/H_2O) to 95% MeCN/ buffer (0.1% TFA/H_2O) for 9 min, then kept the ratio for 6 min, a flow rate of 1.0 mL/min. This method was used to determine the purity for compounds **5-20**.

Spectral copies of ^{1}H NMR, ^{13}C NMR and TOF MS ES^{+} of compounds 4-13, 15 and 19

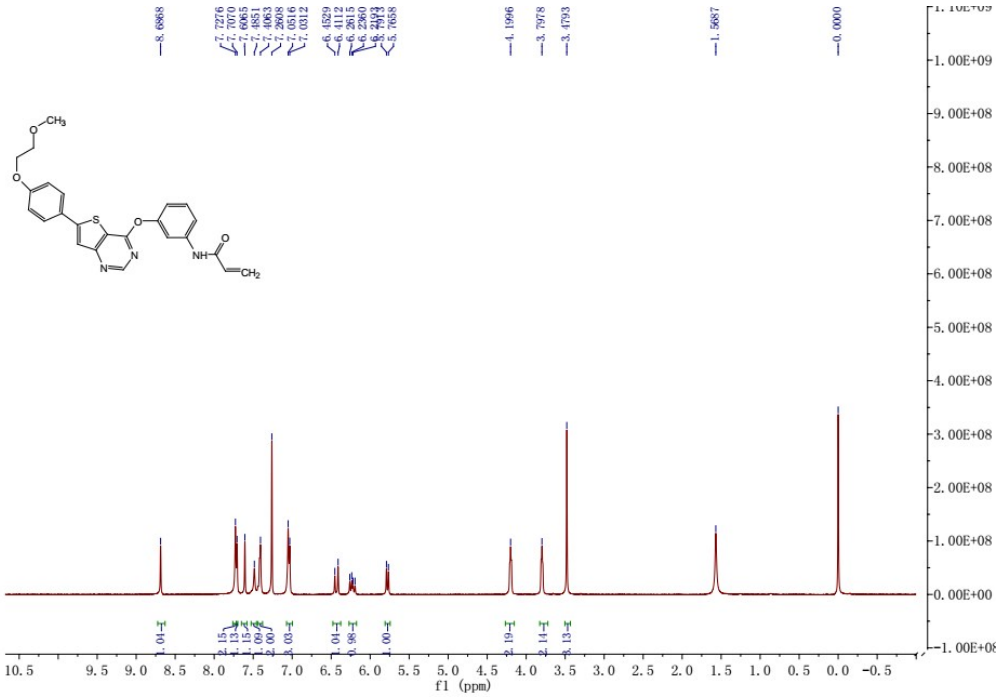
Spectrum of compound **4**

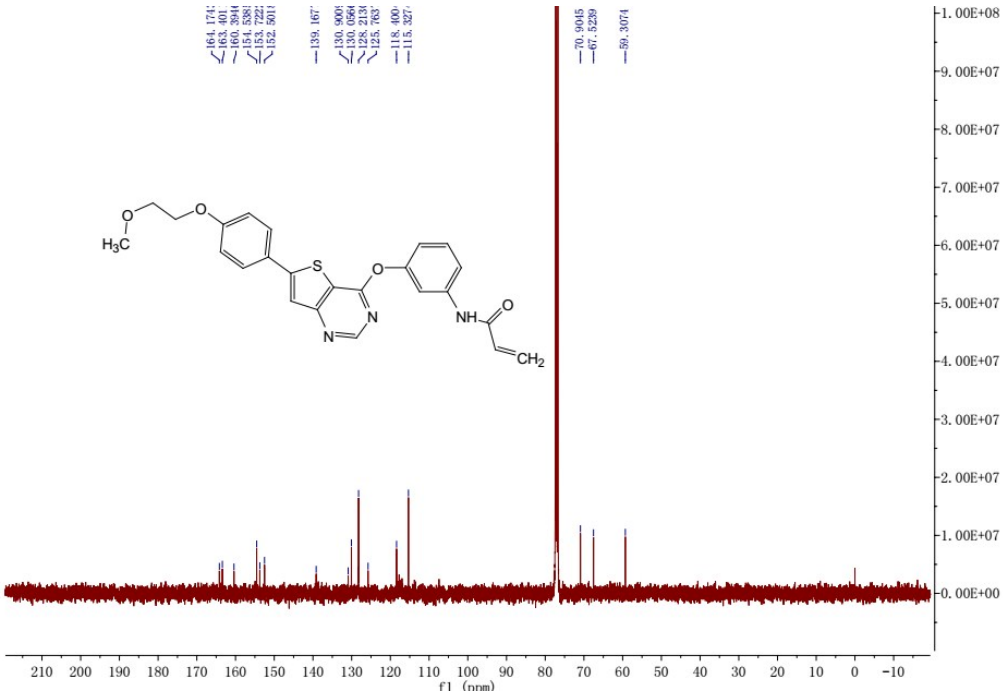


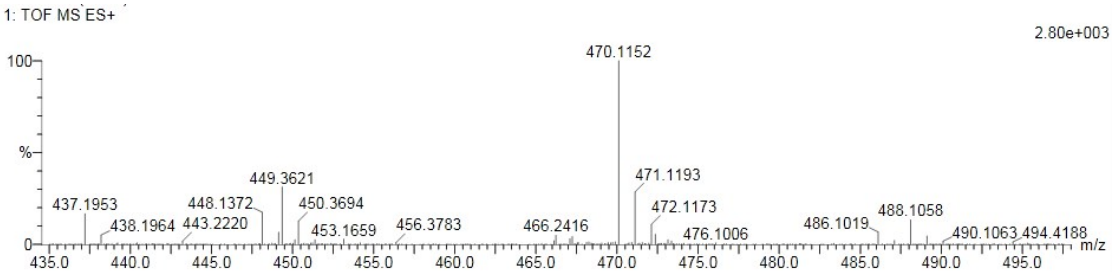




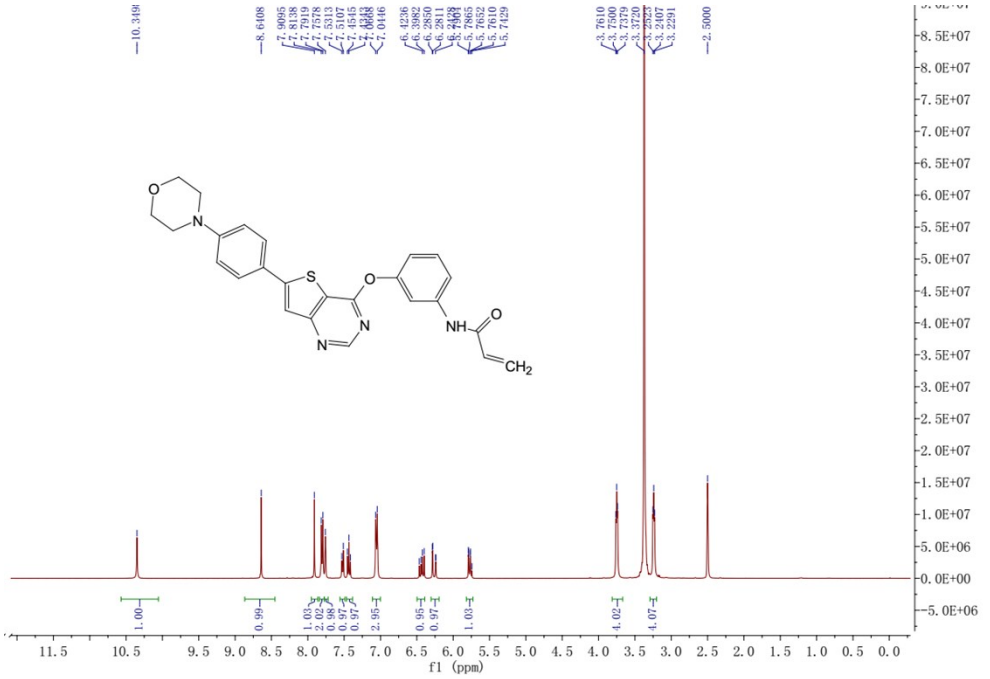
Spectrum of compound **5**

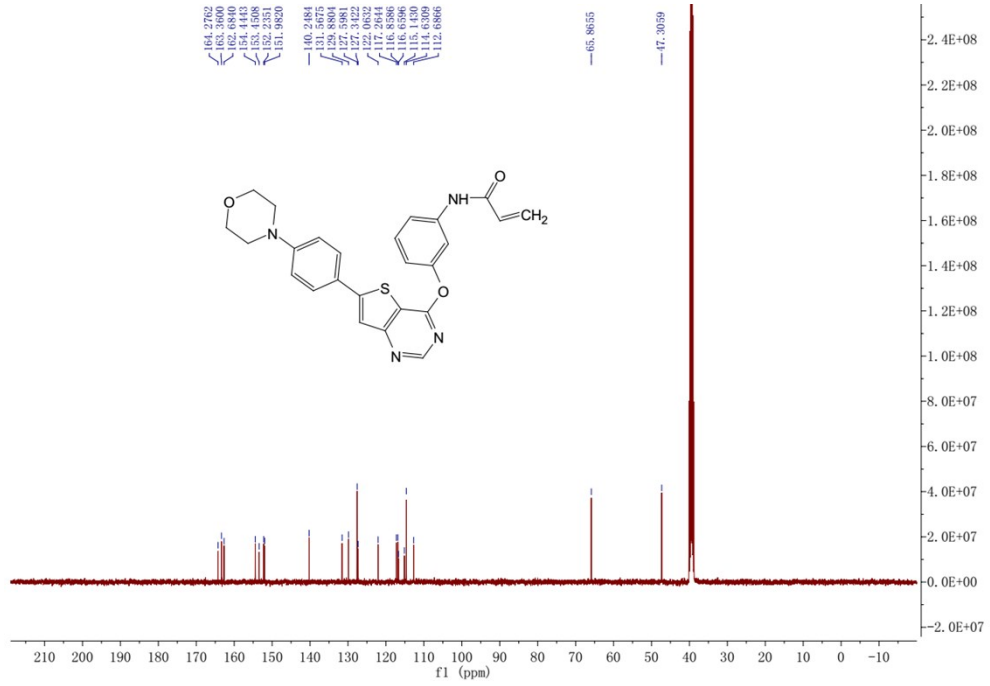


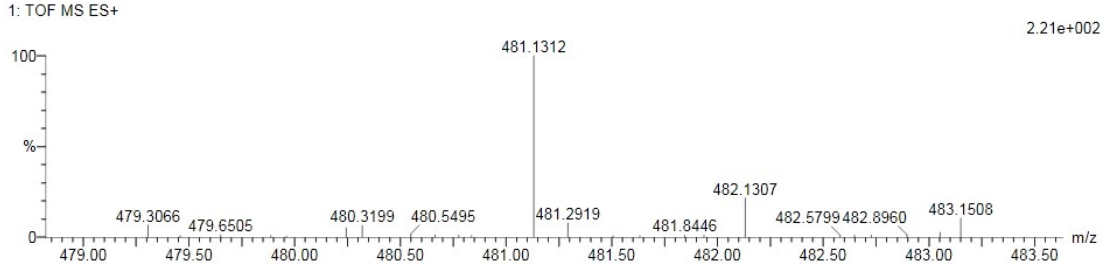




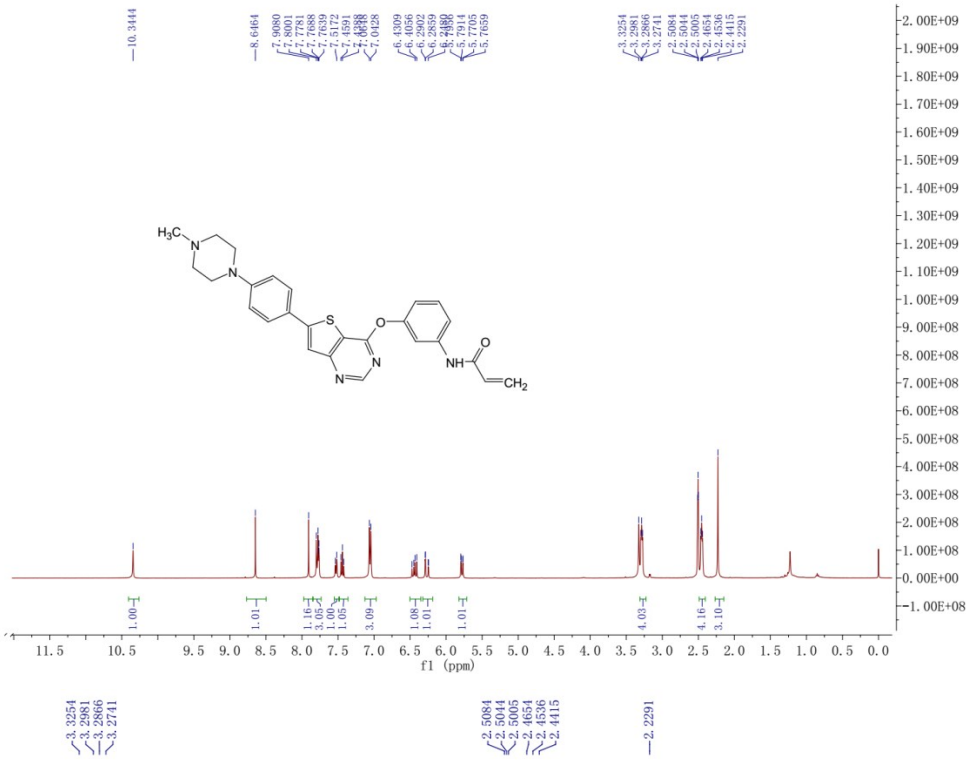
Spectrum of compound **6**

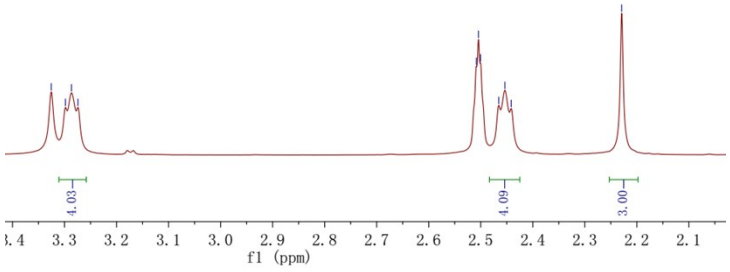


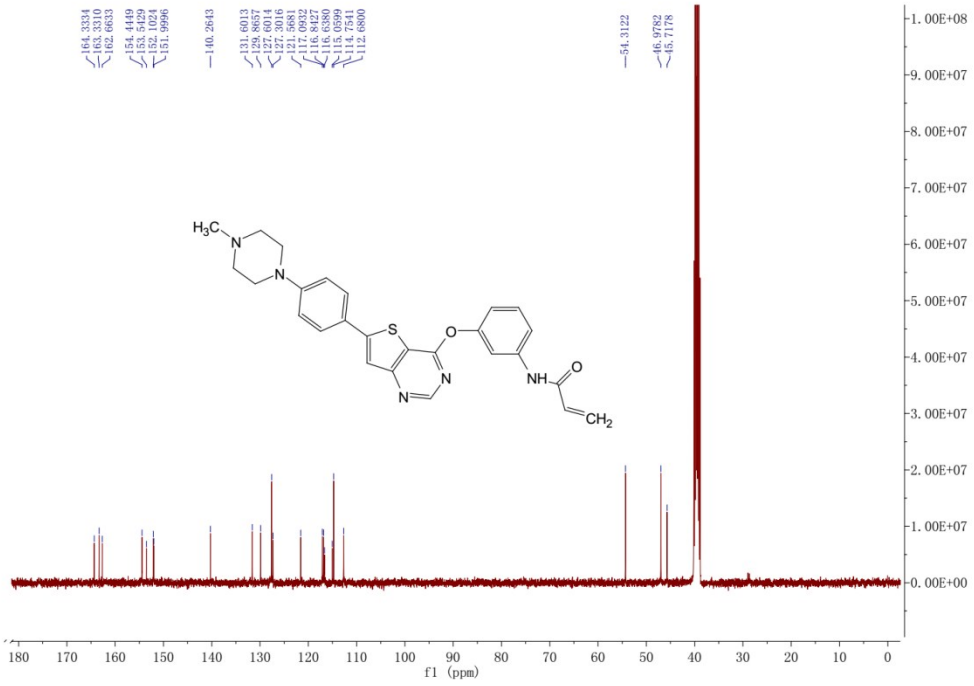




Spectrum of compound **7**



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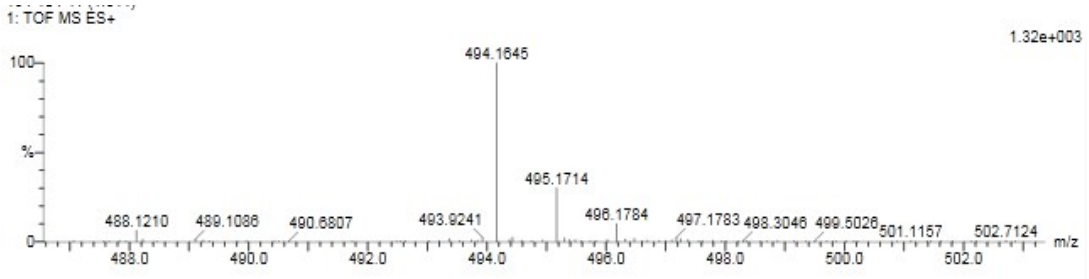
162.6633
154.4449
153.5429
152.1004
151.9996
140.2643
131.6013
129.8657
127.6014
127.2016
121.5681
117.0932
116.8427
116.6380
116.0599
115.7541
112.6800
54.3122
46.9782
45.7178
H3C
N
N
S
O
N
N
NH
O
CH2
1.00E+08
9.00E+07
8.00E+07
7.00E+07
6.00E+07
5.00E+07
4.00E+07
3.00E+07
2.00E+07
1.00E+07
0.00E+00
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


1: TOF MS ES+
1.32e+003
100
%
0
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495.1714
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489.1086
490.6807
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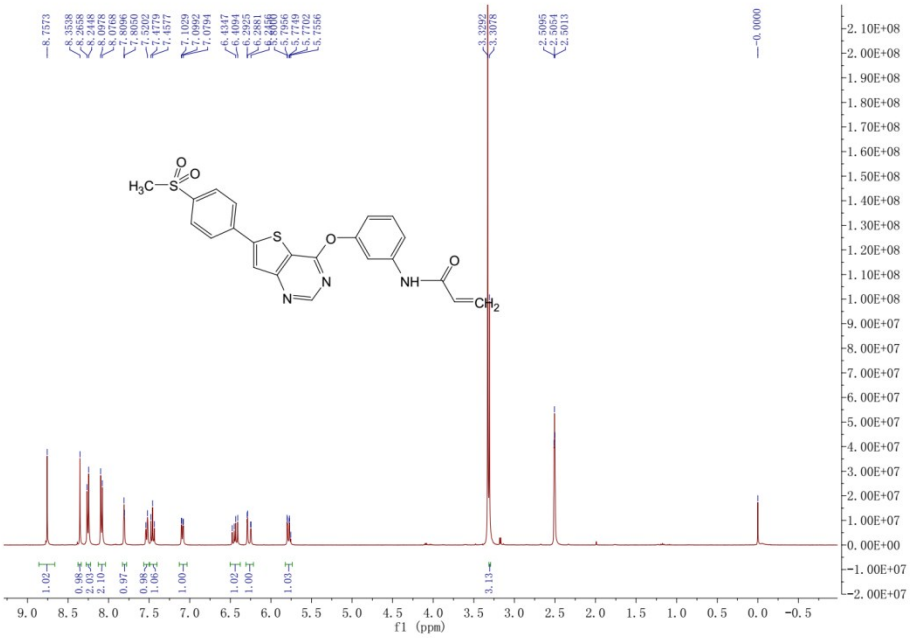
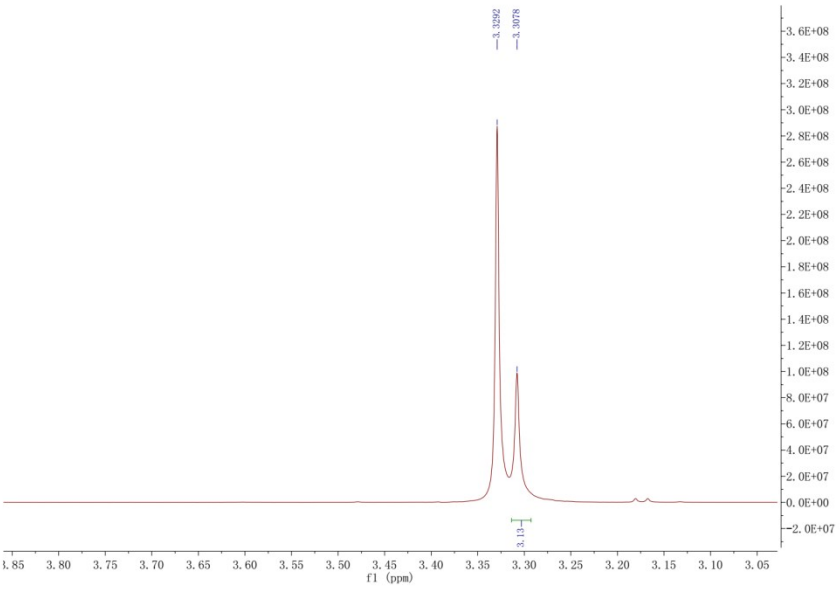
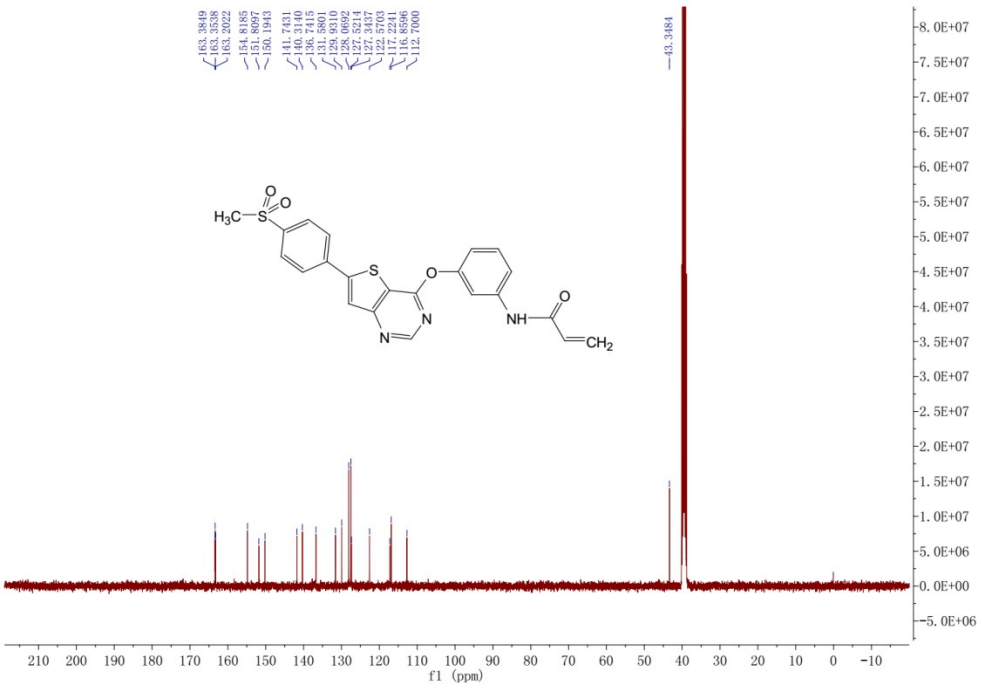
496.1784
497.1783
498.3046
499.5026
501.1157
502.7124
m/z
488.0
490.0
492.0
494.0
496.0
498.0
500.0
502.0

Spectrum of compound **8**



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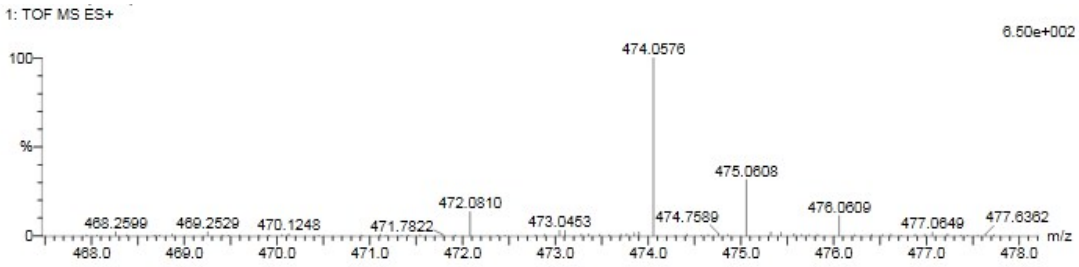
163.3022
154.8185
151.8057
150.1943
141.7431
140.9140
136.7415
131.5801
129.9310
128.0692
127.3214
122.9457
122.5703
117.2241
116.8596
112.7000
43.3484
O
O
H3C
S
S
O
N
N
NH
O
CH2
8.0E+07
7.5E+07
7.0E+07
6.5E+07
6.0E+07
5.5E+07
5.0E+07
4.5E+07
4.0E+07
3.5E+07
3.0E+07
2.5E+07
2.0E+07
1.5E+07
1.0E+07
5.0E+06
0.0E+00
-5.0E+06
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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100
%
0
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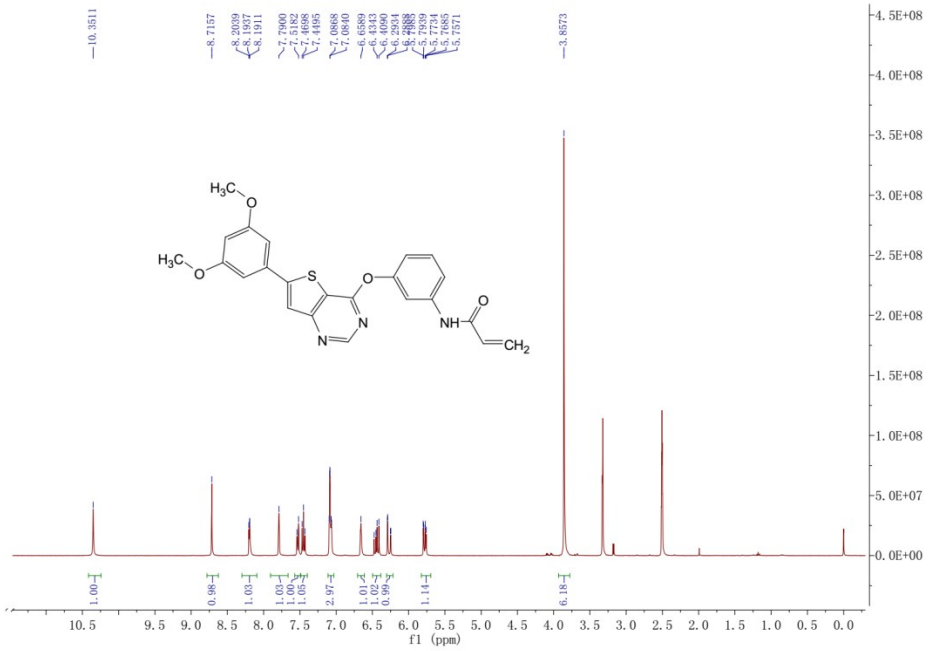
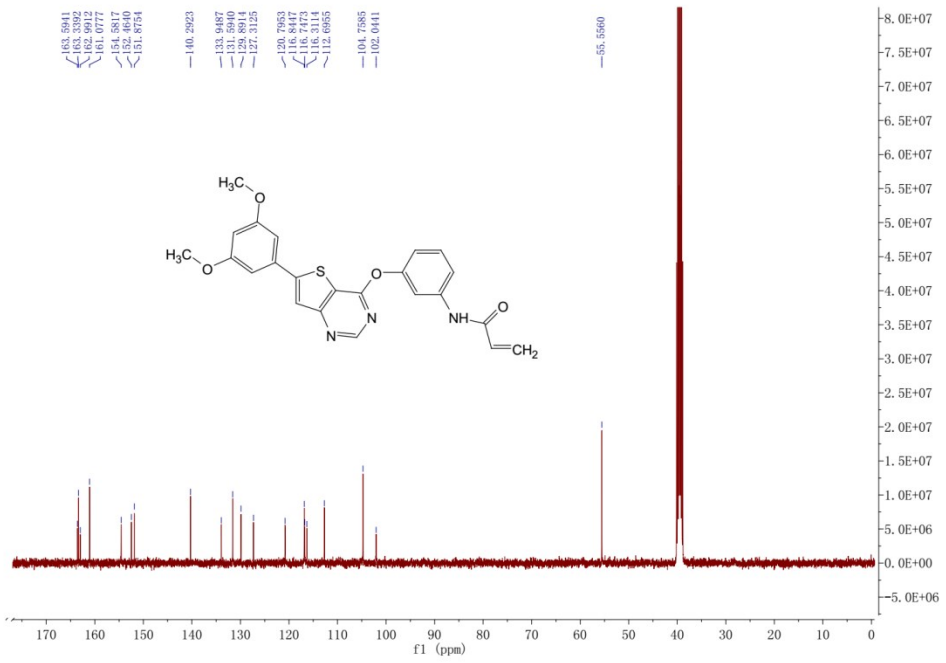
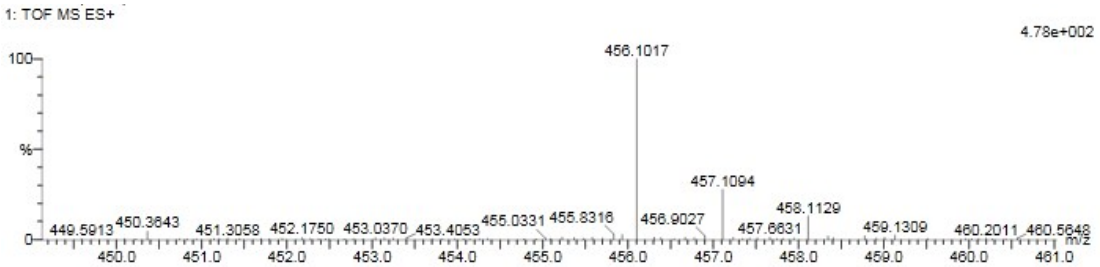
475.0608
472.0810
476.0609
468.2599
469.2529
470.1248
471.7822
473.0453
474.7589
477.0649
477.6362
m/z
468.0
469.0
470.0
471.0
472.0
473.0
474.0
475.0
476.0
477.0
478.0

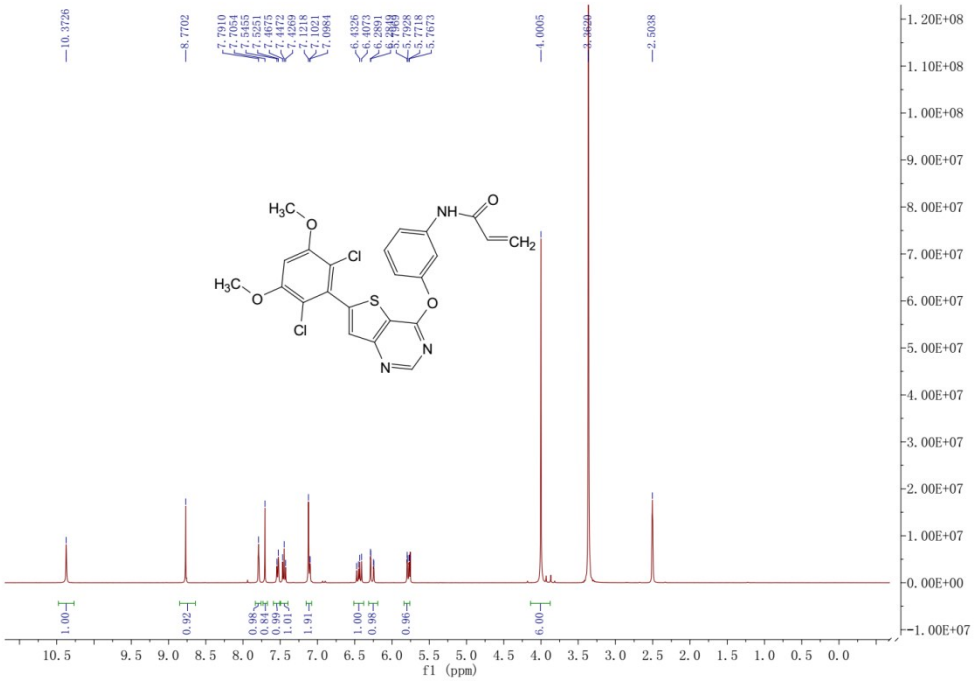
Spectrum of compound **9**

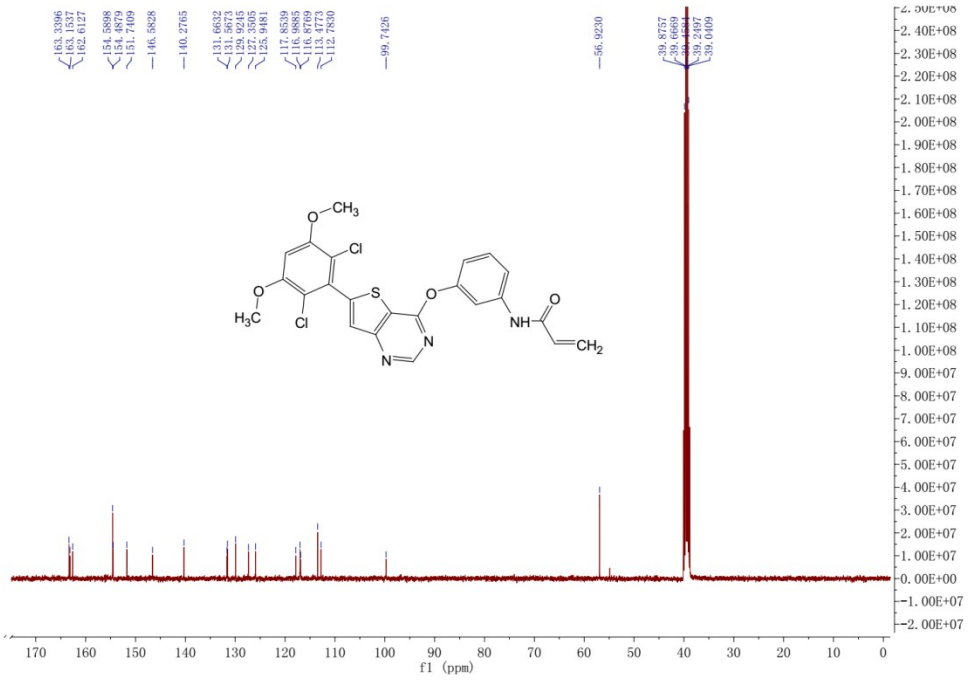


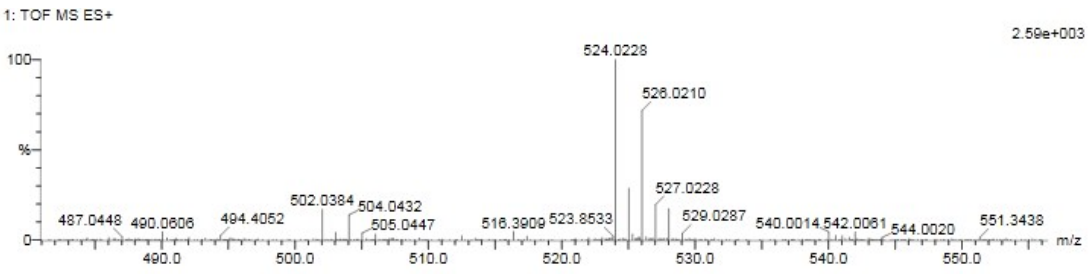




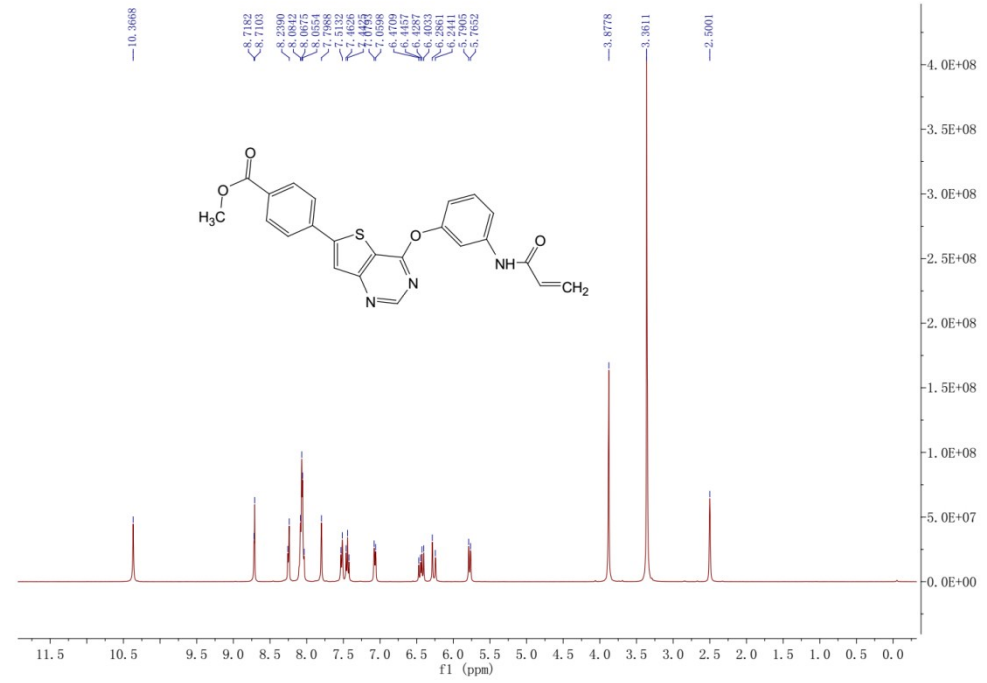
Spectrum of compound **10**

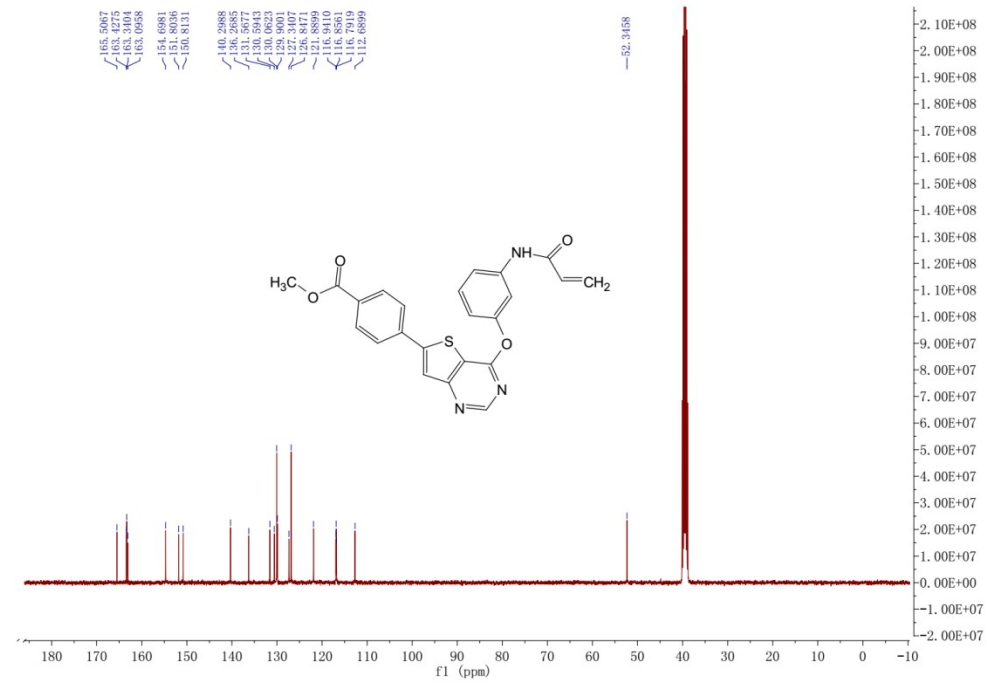


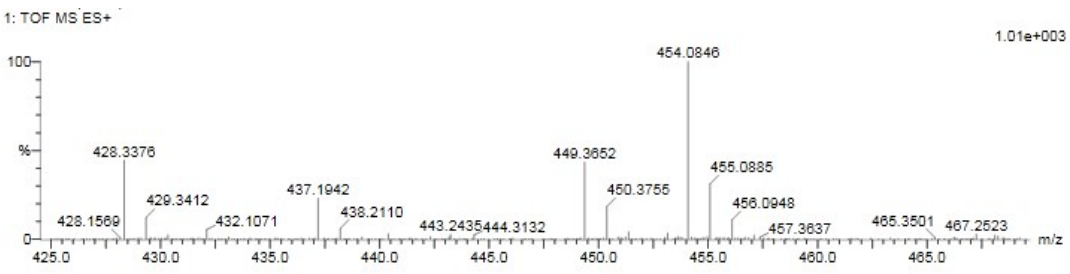




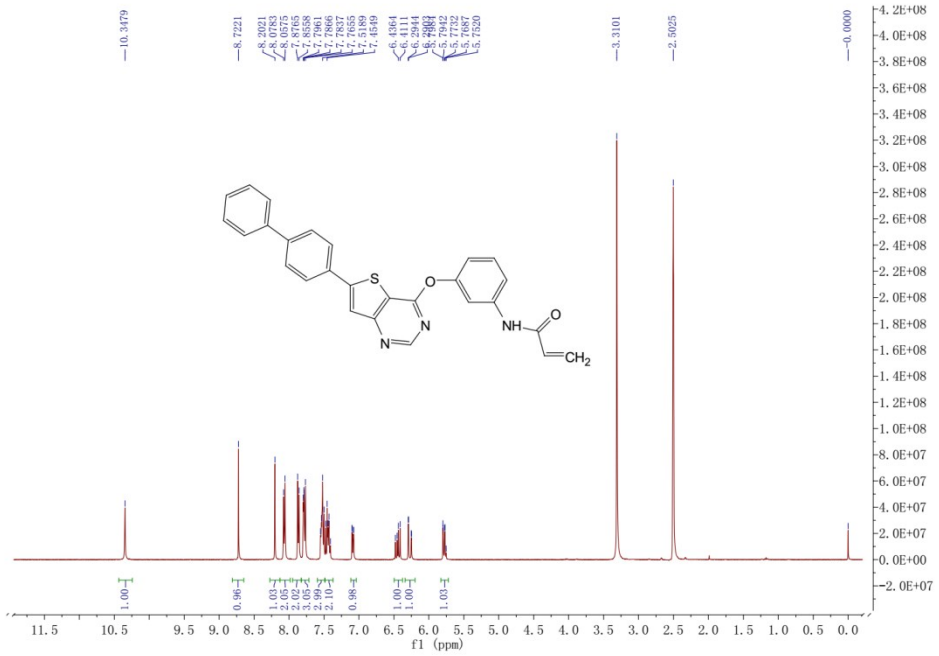
Spectrum of compound **11**

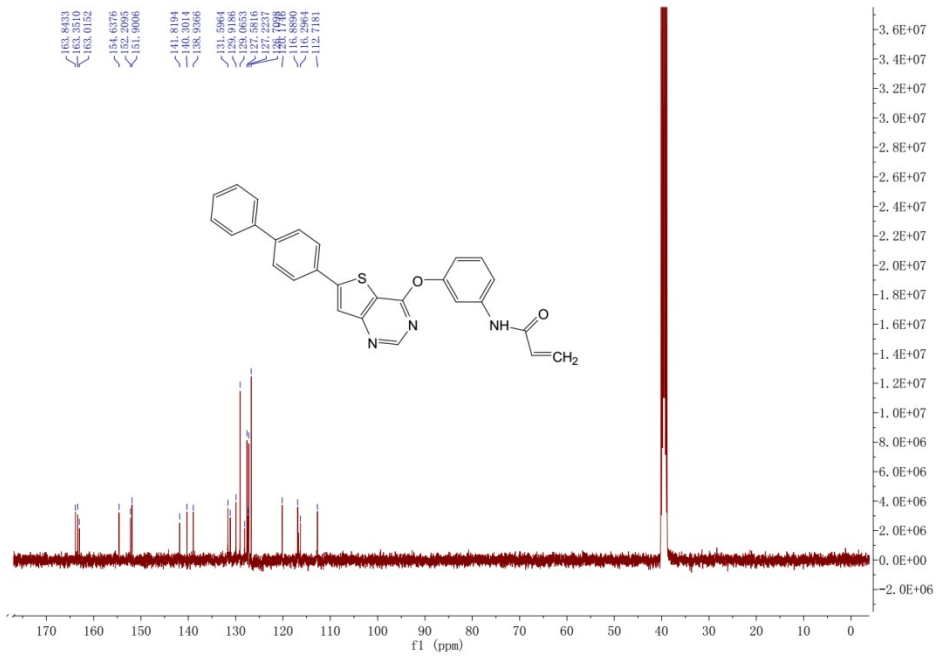


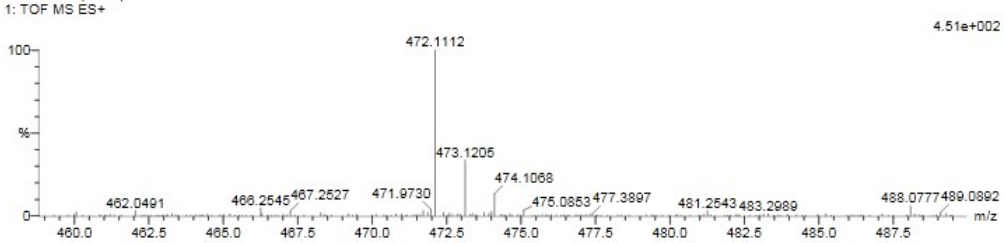




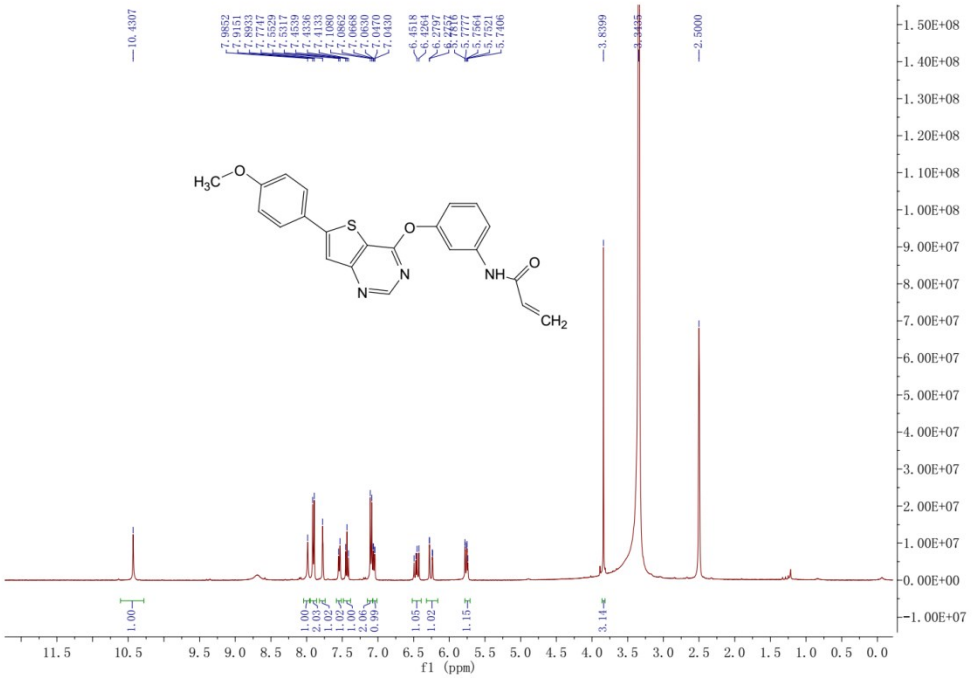
Spectrum of compound **12**

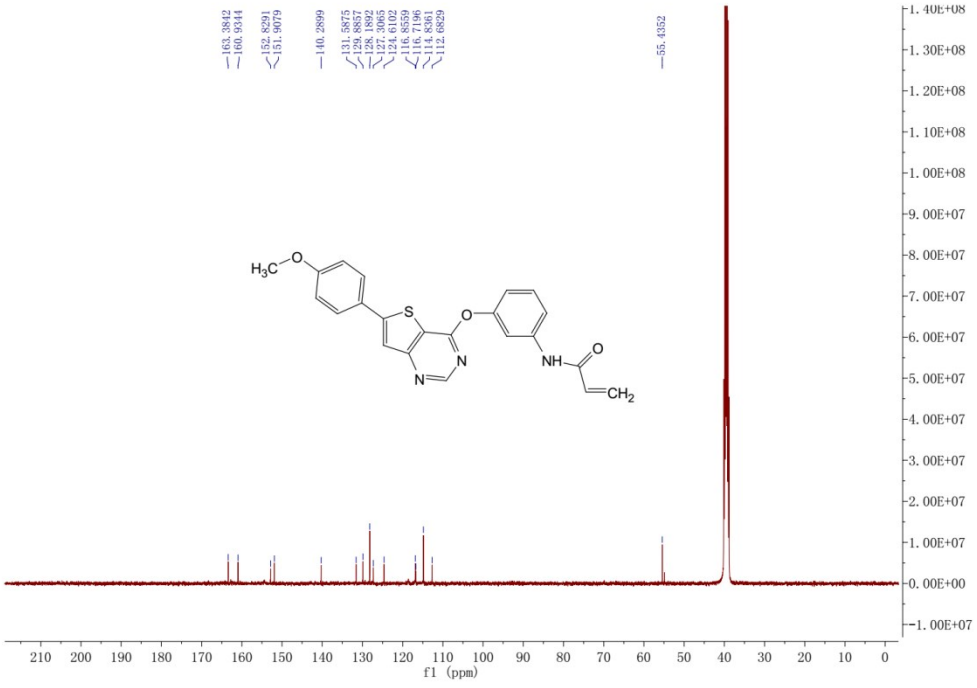


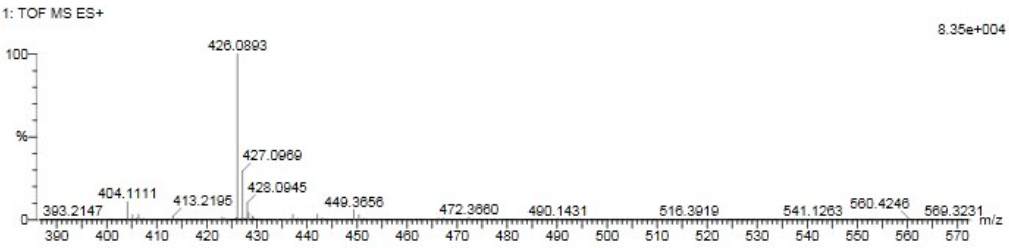




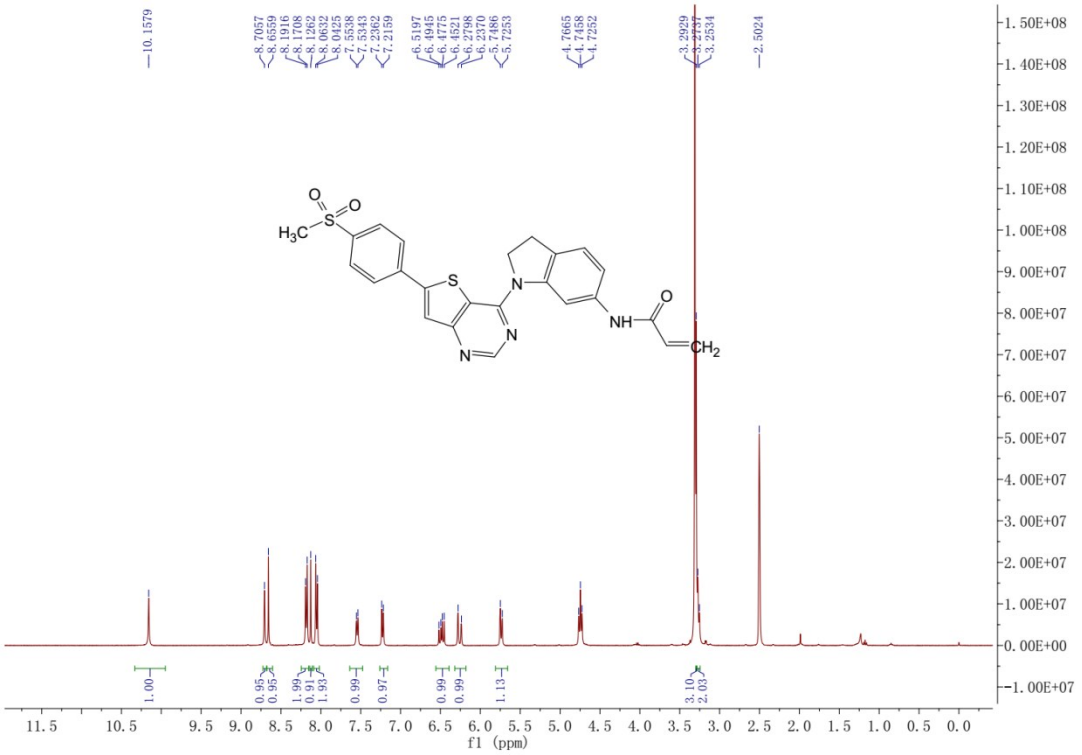
Spectrum of compound **13**

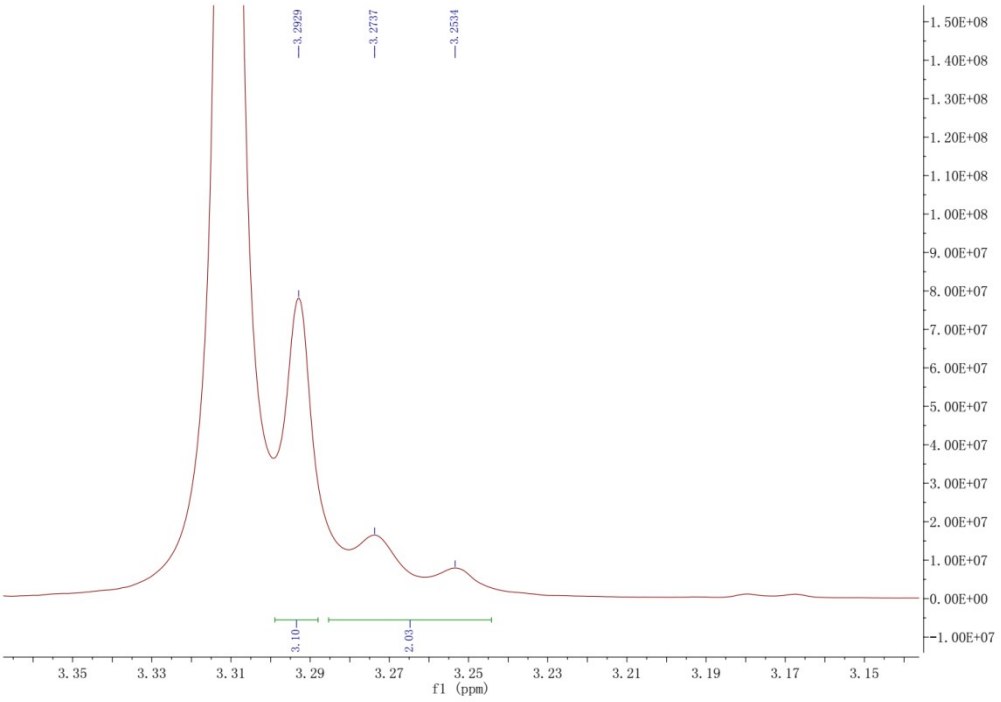


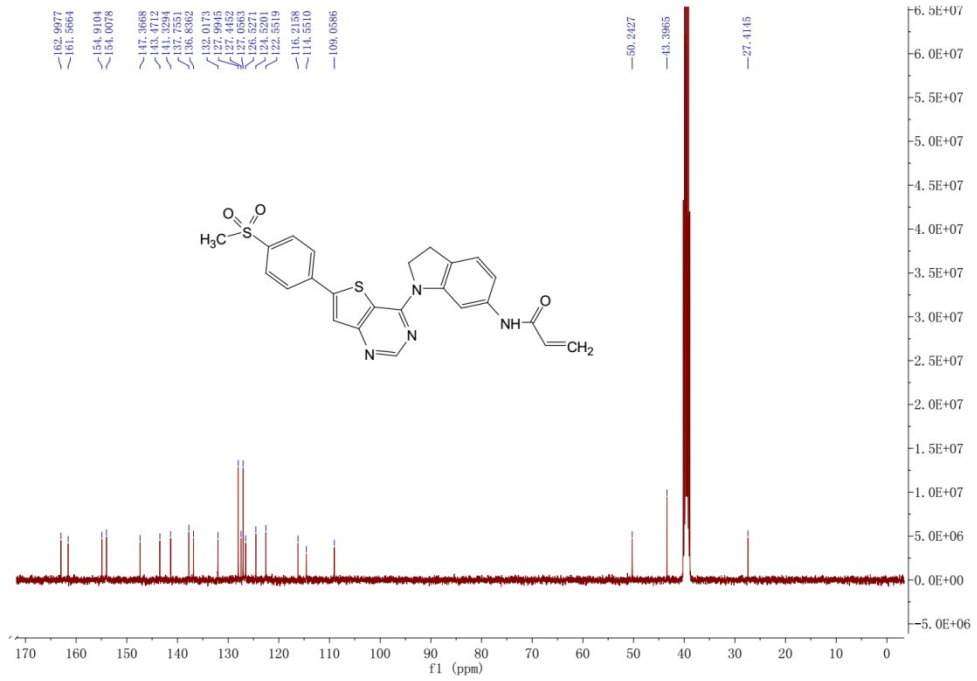


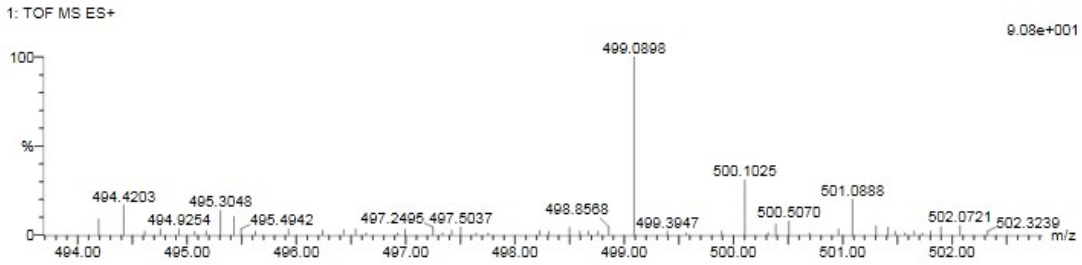


Spectrum of compound **15**

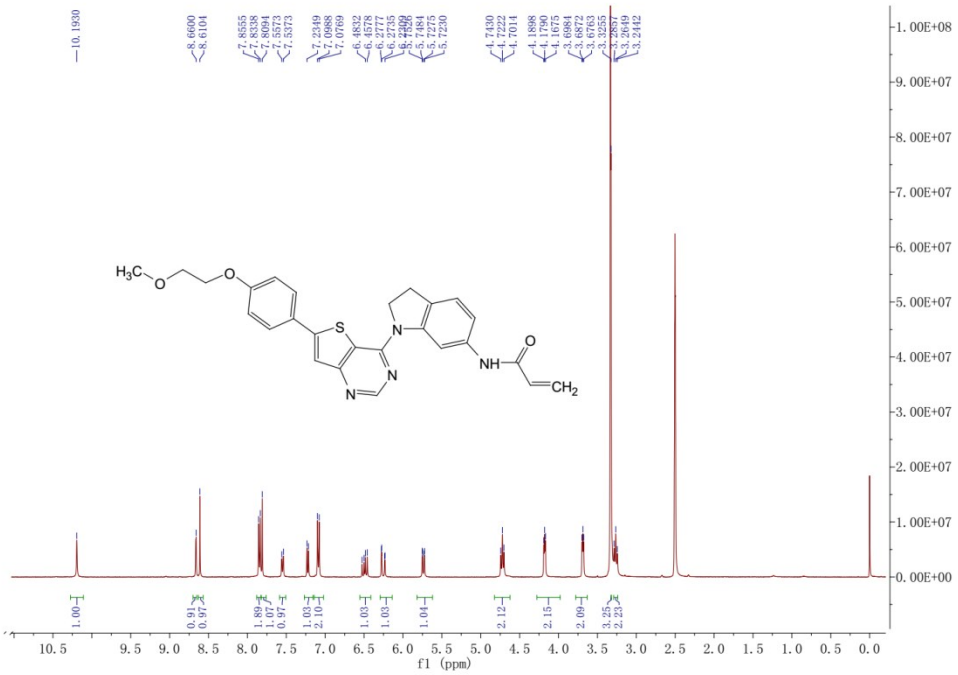


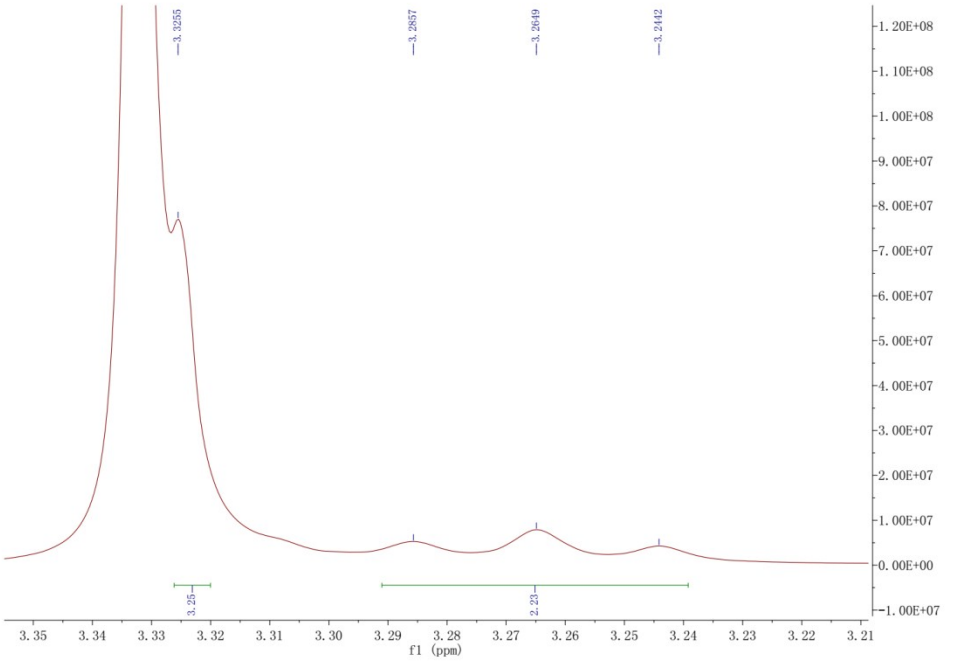


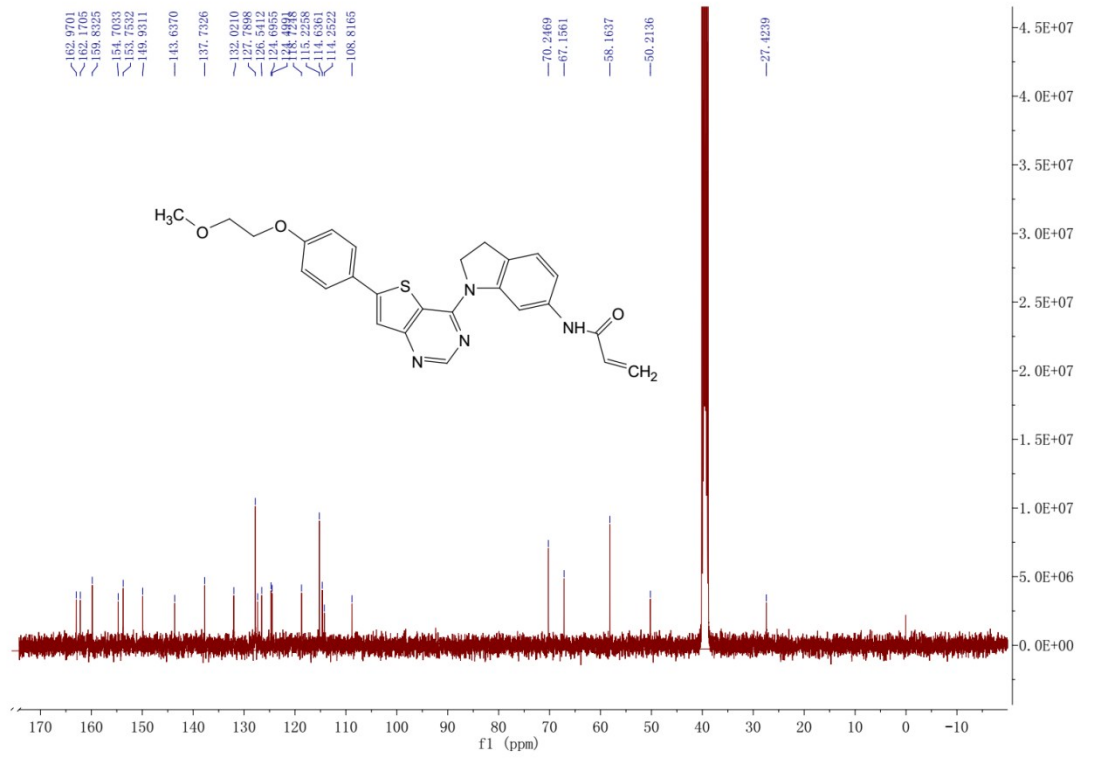

162.9977
161.5664
154.9104
154.0078
147.3668
143.4712
141.3294
137.7551
136.8362
132.0173
127.9945
127.4452
127.1065
126.5271
124.5201
122.5519
116.2158
114.5510
109.0586
50.2427
43.3965
27.4145
6.5E+07
6.0E+07
5.5E+07
5.0E+07
4.5E+07
4.0E+07
3.5E+07
3.0E+07
2.5E+07
2.0E+07
1.5E+07
1.0E+07
5.0E+06
0.0E+00
-5.0E+06
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
O
O
S
H3C
S
N
N
N
NH
O
CH2


1: TOF MS ES+
9.08e+001
100
%
0
499.0898
500.1025
501.0888
494.4203
495.3048
494.9254
495.4942
497.2495
497.5037
498.8568
499.3947
500.5070
502.0721
502.3239
m/z
494.00
495.00
496.00
497.00
498.00
499.00
500.00
501.00
502.00

Spectrum of compound **19**






162.9701
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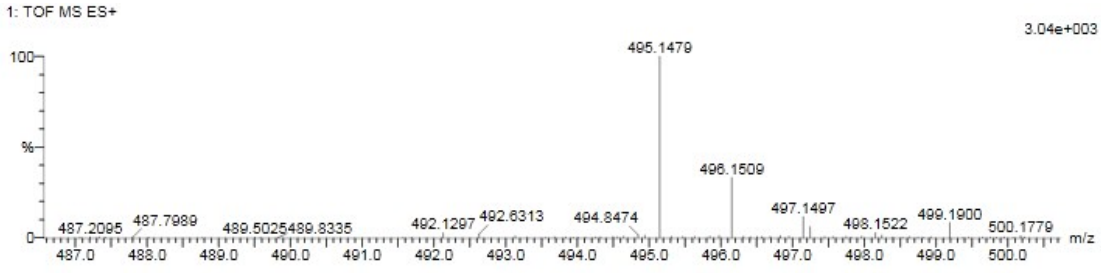
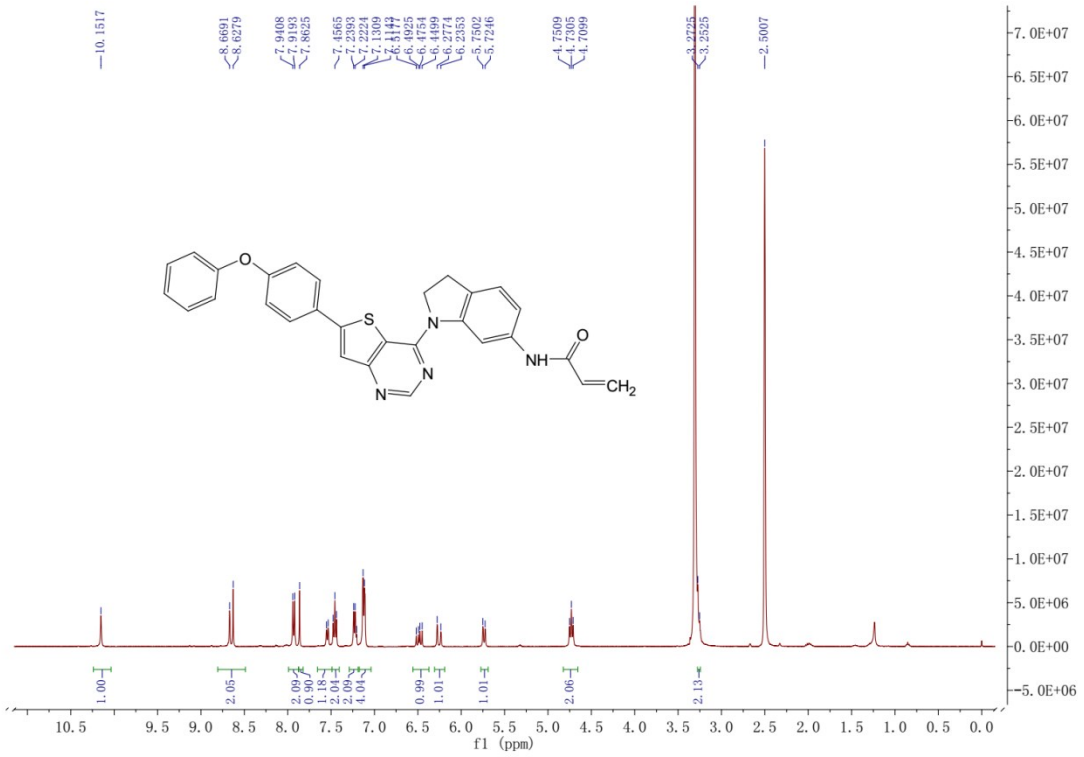
154.7033
153.7532
149.9311
143.6370
137.7326
132.0210
127.7898
126.5412
124.6955
118.4291
115.2258
114.6361
114.2522
108.8165
70.2469
67.1561
58.1637
50.2136
27.4239
H3C
O
O
S
N
N
N
NH
O
CH2
4.5E+07
4.0E+07
3.5E+07
3.0E+07
2.5E+07
2.0E+07
1.5E+07
1.0E+07
5.0E+06
0.0E+00
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

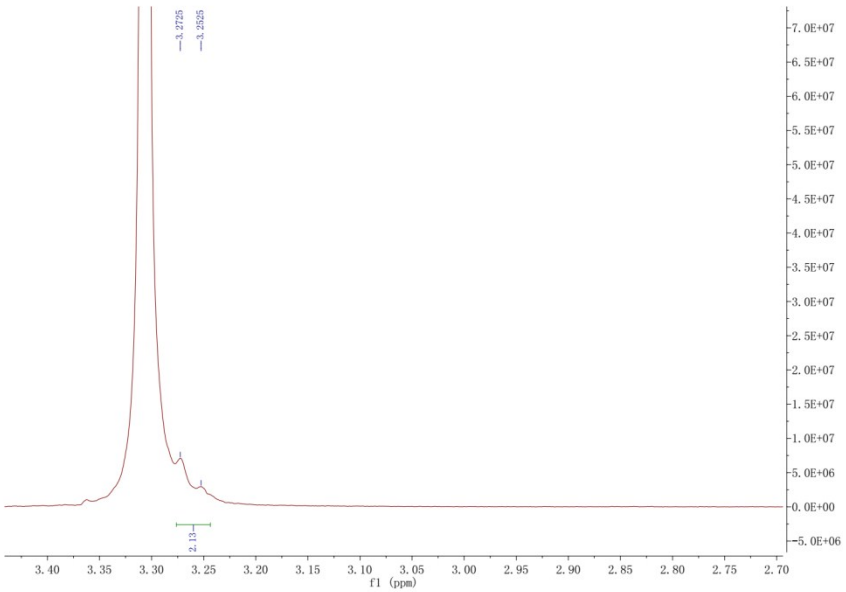

1: TOF MS ES+
3.04e+003
100
%
0
495.1479
496.1509
497.1497
487.2095
487.7989
489.5025489.8335
492.1297
492.6313
494.8474
498.1522
499.1900
500.1779
m/z
487.0 488.0 489.0 490.0 491.0 492.0 493.0 494.0 495.0 496.0 497.0 498.0 499.0 500.0

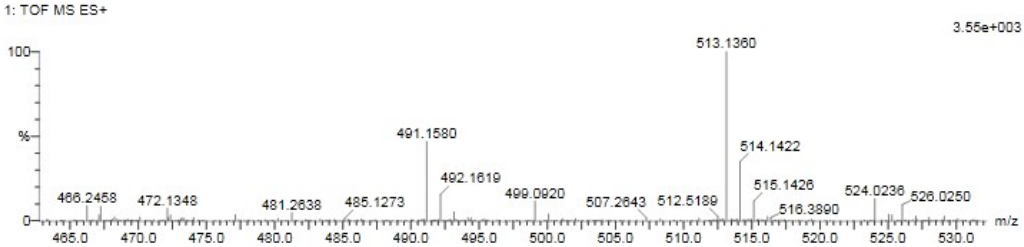
Spectral copies of ^{1}H NMR and TOF MS ES^{+} of compounds 14, 16, 17, 18 and 20

(Compounds **14, 16, 17, 18 and 20** have poor solubilities and their ^{13}C NMR data were hard to get**)**

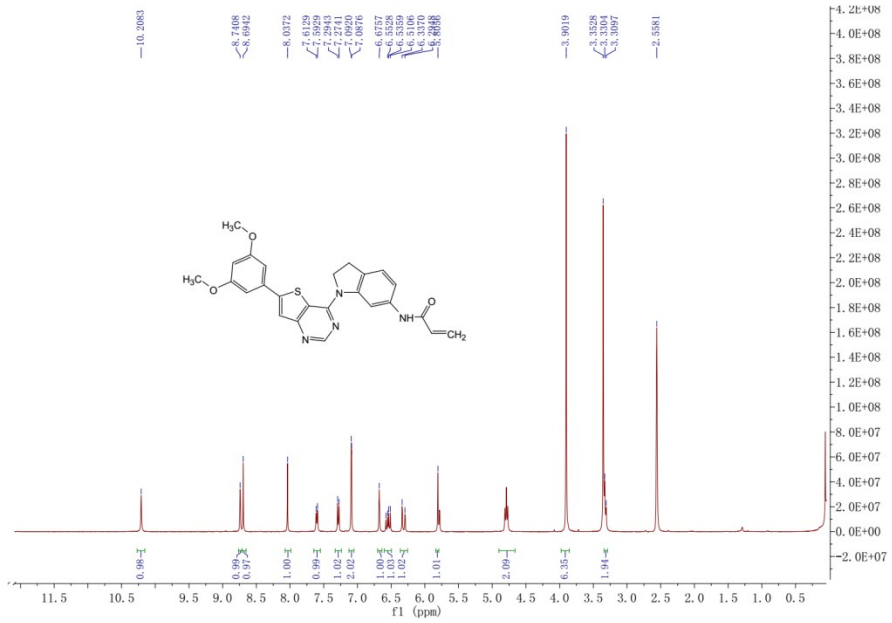
Spectrum of compound **14**

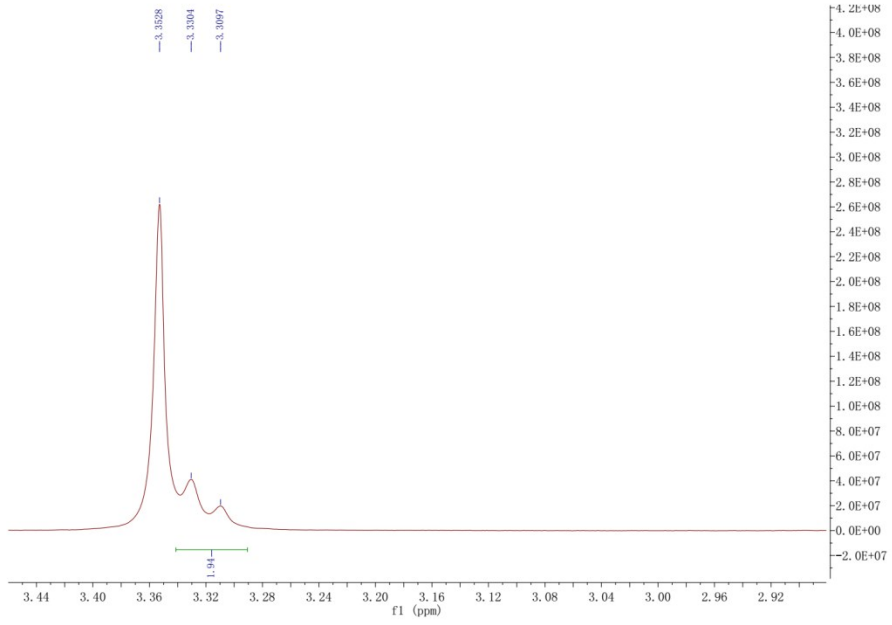


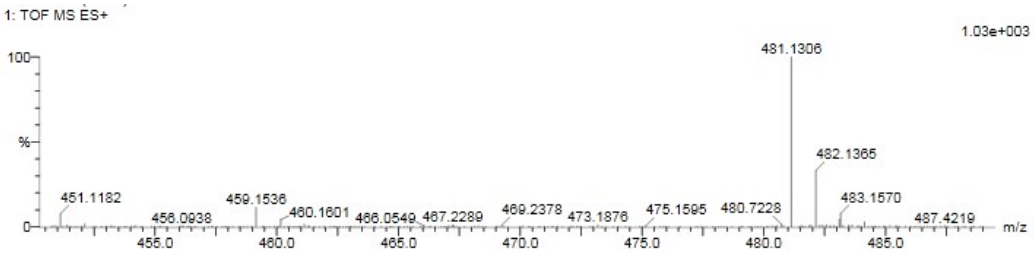




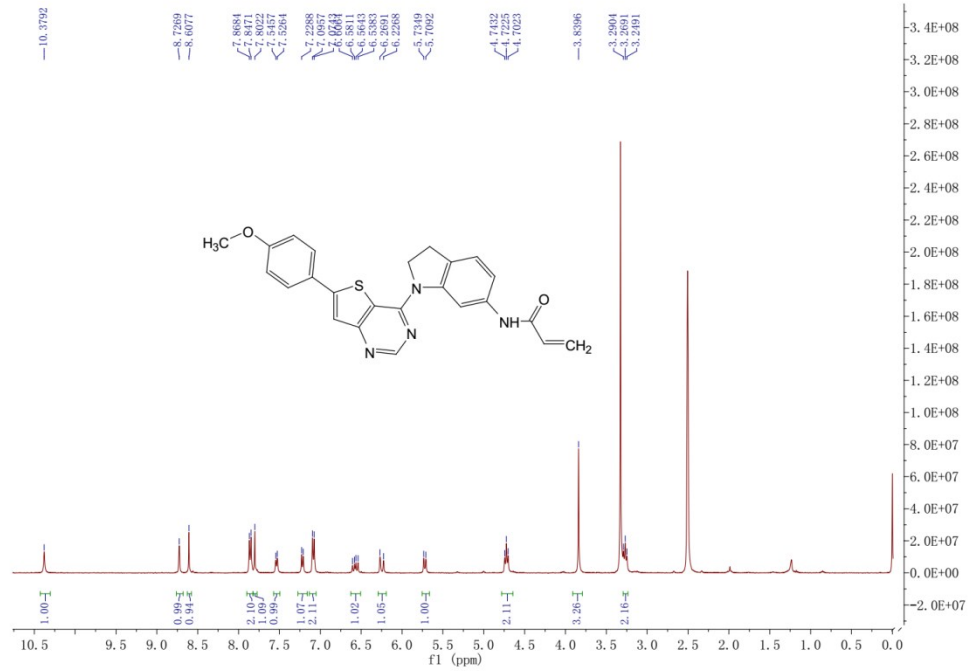
Spectrum of compound **16**

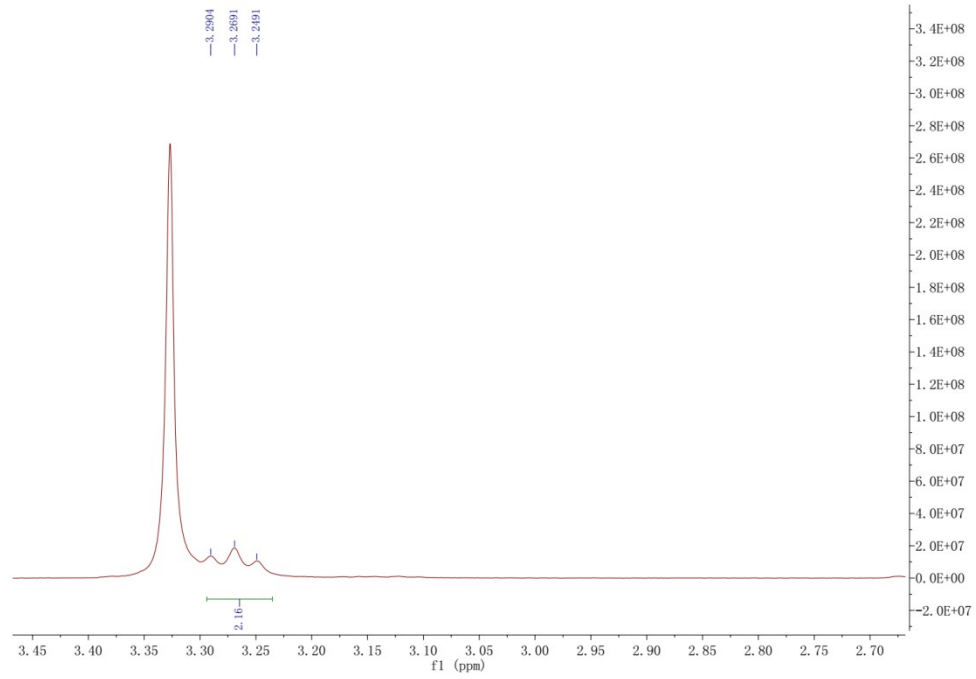


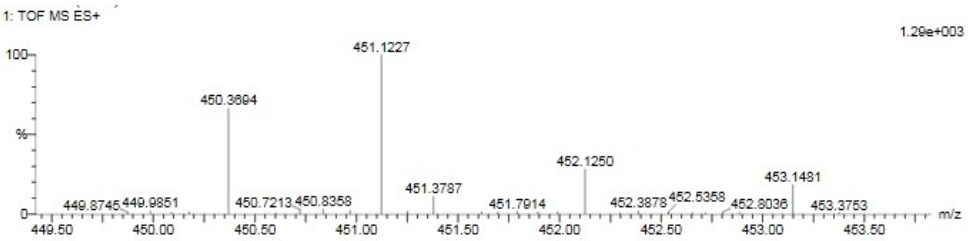




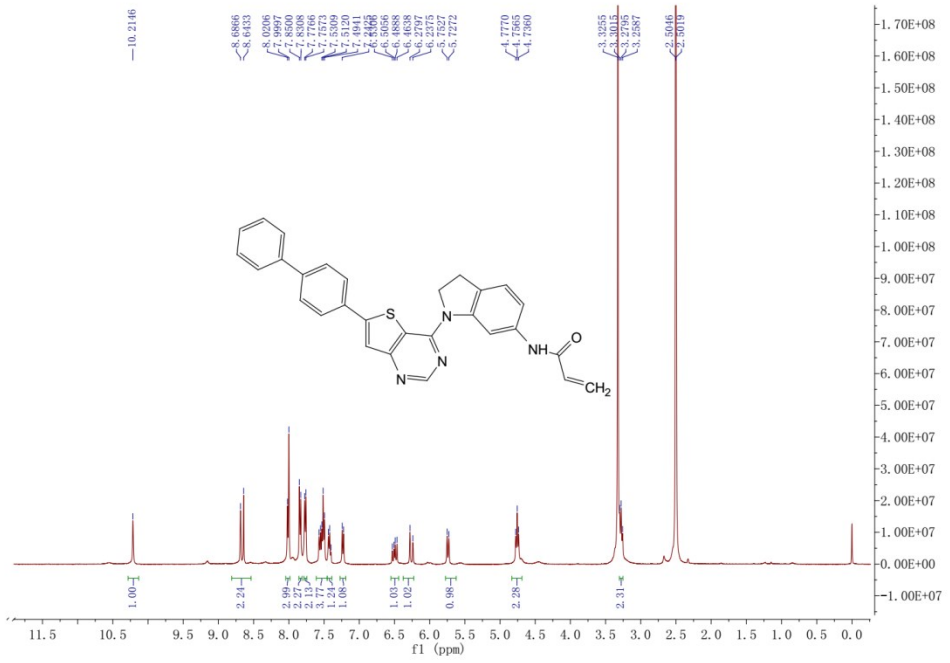
Spectrum of compound **17**

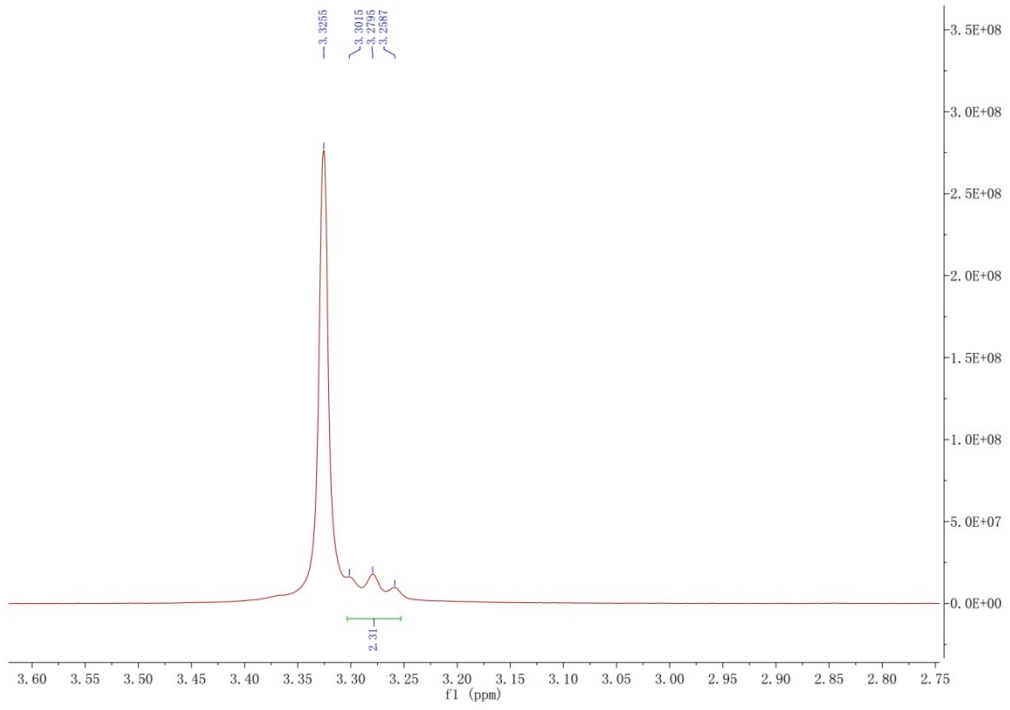


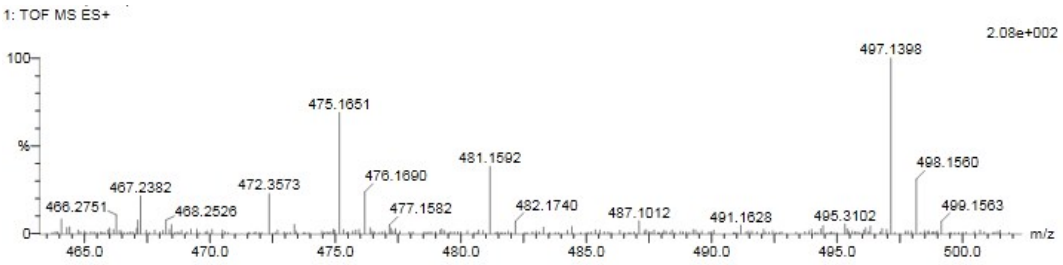




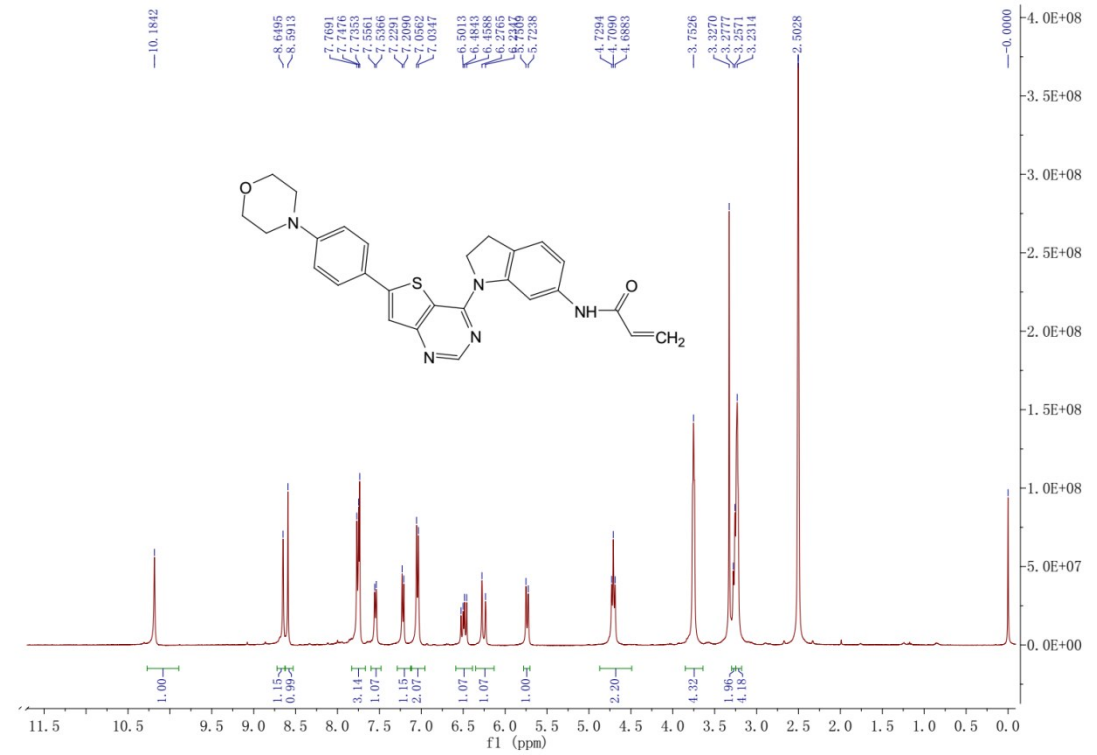
Spectrum of compound **18**

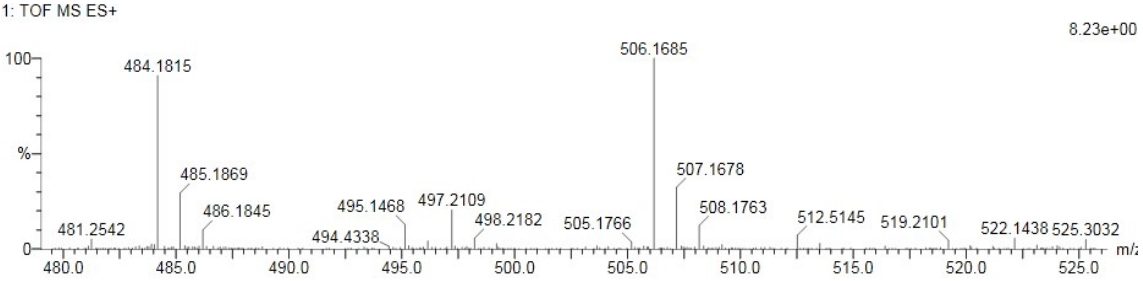






Spectrum of compound **20**





The IC_{50} curves of compounds 7, 8 and Olmutinib against BTK and EGFR

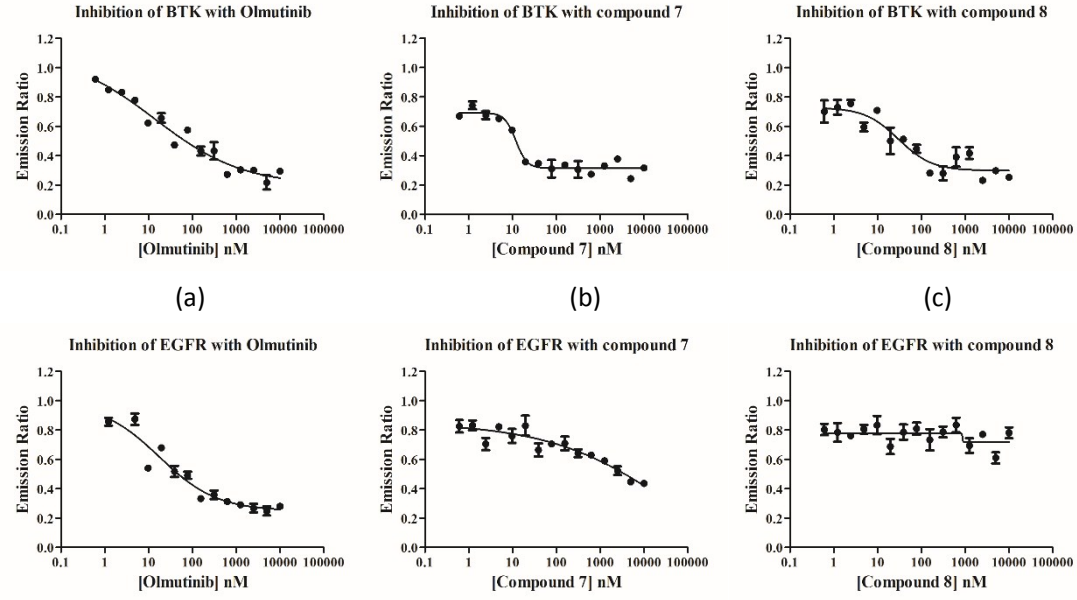


Fig. S1. The inhibition of compounds **7**, **8** and Olmutinib against BTK and EGFR: (a) The inhibition of Olmutinib against BTK; (b) The inhibition of compound **7** against BTK; (c) The inhibition of compound **8** against BTK; (d) The inhibition of Olmutinib against EGFR; (e The inhibition of compound **7** against EGFR; (f) The inhibition of compound **8** against EGFR.